Answer 1:

Bibliographic Information

Simultaneously targeting CD45 significantly increases cytotoxicity of the anti-CD33 immunoconjugate, gemtuzumab ozogamicin, against acute myeloid leukemia (AML) cells and improves survival of mice bearing human AML xenografts. Walter, Roland B.; Boyle, Kelli M.; Appelbaum, Frederick R.; Bernstein, Irwin D.; Pagel, John M. Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA. Blood (2008), 111(9), 4813-4816. Publisher: American Society of Hematology, CODEN: BLOOAW ISSN: 0006-4971. Journal written in English. CAN 148:535773 AN 2008:540832 CAPLUS

Abstract

Targeting CD33 or CD45 is currently exploited for immunotherapy of acute myeloid leukemia (AML). Gemtuzumab ozogamicin (GO), an immunoconjugate of an anti-CD33 antibody that facilitates cellular uptake of a toxic calicheamicin-γ1 deriv., induces complete remissions in a subset of patients with AML. We herein tested whether simultaneous targeting of CD45 could improve GO cytotoxicity against AML cell lines and primary AML cells. We found that the anti-CD45 antibody, BC8, dose-dependently increased cytotoxicity induced by GO, and, to a lesser degree, free calicheamicin-γ1. BC8 promoted CD33 endocytosis, suggesting that its effect on GO cytotoxicity may be, at least partly, due to increased uptake and intracellular GO availability. Finally, compared with either agent alone, BC8 combined with GO resulted in marked tumor growth inhibition and superior survival rates of mice bearing human AML xenografts. These data suggest that further study of this antibody combination for clin. use in AML is warranted.

Answer 2:

Bibliographic Information

Potent and specific antitumor efficacy of CMC-544, a CD22-targeted immunoconjugate of calicheamicin, against systemically disseminated B-cell lymphoma. DiJoseph, John F.; Goad, Mary E.; Dougher, Maureen M.; Boghaert, Erwin R.; Kunz, Arthur; Hamann, Philip R.; Damle, Nitin K. Oncology Discovery and Chemical and Screening Sciences, Wyeth Research, Pearl River, NY, USA. Clinical Cancer Research (2004), 10(24), 8620-8629. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 142:390643 AN 2004:1150196 CAPLUS

Abstract

CMC-544 is a CD22-targeted immunoconjugate of calicheamicin and exerts a potent cytotoxic effect against CD22+ B-cell lymphoma. This study evaluated antitumor efficacy of CMC-544 against systemically disseminated B-cell lymphoma. Scid mice received i.v. injections of CD22+ Ramos B-cell lymphoma cells for their systemic dissemination. CMC-544, G5/44, CD33-targeted CMA-676 (control conjugate) or rituximab were given i.p. 3, 9, 15, or 21 days after B-cell lymphoma dissemination. Diseased mice were monitored daily for hind-limb paralysis and death. Histopathol. examn. of CMC-544-treated and vehicle-treated diseased mice was also performed. Mice with disseminated B-cell lymphoma developed hind-limb paralysis within 35 days. When given up to 15 days after B-cell lymphoma dissemination, CMC-544 extended survival of the diseased mice to >100 days, and these mice were considered cured. CMC-544 was efficacious when given during both the early initiation phase and the late established phase of the disease. A single dose of CMC-544 was effective in delaying the occurrence of hind-limb paralysis. In contrast, neither CMA-676 nor unconjugated G5/44 was effective. Rituximab was effective when given early in the disease process but not when the disease was established. Histopathol. anal. revealed B-cell lymphoma infiltration in brain, spinal cord, bone marrow, and kidney in vehicle-treated but not in CMC-544-treated diseased mice. Consistent with its efficacy against the disseminated B-cell lymphoma, CMC-544 also caused regression of established Ramos B-cell lymphoma xenografts in scid mice. CMC-544 confers strong therapeutic activity against systemic disseminated B-cell lymphoma and protects mice from hind-limb paralysis and death. These results support clin. evaluation of CMC-544 in the treatment of CD22+ lymphoid malignancies.